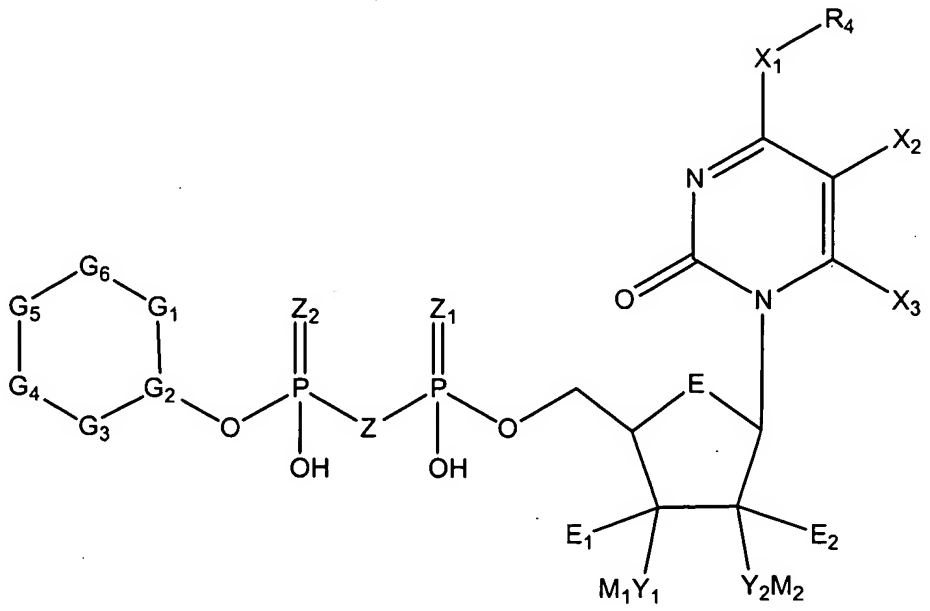
THE AMENDMENTS

1. (Currently Amended) A method of reducing intraocular pressure comprising administering to a subject a pharmaceutical composition comprising an effective amount of a compound of Formula I, its ~~diasteromers~~ diastereomers, enantiomers, tautomers, or pharmaceutically acceptable salts thereof:



wherein:

X_1 = O~~, NR, S, CF_2, CF_3 or CN with the proviso that when X_1 = CF_3 or CN, then R_4 is absent; or X_1 represents a bond from the pyrimidine ring to R_4~~ or S;

X_2 = H, F, Cl, Br, I, CN~~, OR_8, SR_8, NR_9R_{13}, CF_3,~~ or alkyl~~, cycloalkyl, arylalkyl, aryl, arylalkenyl, arylalkynyl, $C(O)R_{16}$, $C(O)OR_{17}$, $C(O)NR_{16}R_{18}$ or heterocycle of 5 to 7 members~~;

X_3 = H~~, CN, OR_{19}, SR_{19}, $NR_{23}R_{28}$, CF_3, alkyl, cycloalkyl, $C(O)R_{32}$, $C(O)OR_{33}$, $C(O)NR_{34}R_{35}$, arylalkyl, aryl, arylalkenyl, arylalkynyl, or a heterocycle of 5 to 7 members~~;

~~R = H, OR_1, alkyl, cycloalkyl, arylalkyl, aryl, $C(O)R_2$, $C(O)OR_3$ or $C(O)NR_1R_2$;~~

~~R_1, R_7, R_{10}, R_{22}, R_{24}, R_{27}, R_{31}, R_{33} and R_{35} are each independently H, alkyl, cycloalkyl, arylalkyl or aryl;~~

~~R_2 = H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members; or~~

~~R_1 and R_2 taken together can form a heterocyclic ring of 5 to 7 members;~~

~~R_3, R_6, R_8, R_{12}, R_{15}, R_{17}, R_{21}, R_{26} and R_{30} are independently alkyl, cycloalkyl, arylalkyl or aryl;~~

~~R_4 = H, alkyl, cycloalkyl, arylalkyl, aryl, heterocyclic ring of 5 to 7 members, $C(O)R_5$, $C(O)OR_6$ or $C(O)NR_5R_7$;~~

~~R_5, R_{11}, R_{14}, R_{16}, R_{18}, R_{20}, R_{25}, R_{29}, R_{32} and R_{34} are independently H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;~~

~~R_9 = H, OR_{10}, alkyl, cycloalkyl, arylalkyl, aryl, $C(O)R_{11}$, $C(O)OR_{12}$ or $C(O)NR_{10}R_{11}$;~~

~~R_{13} = H, alkyl, cycloalkyl, arylalkyl, aryl, $C(O)R_{14}$ or $C(O)OR_{15}$;~~

~~R_{19} = alkyl, cycloalkyl, arylalkyl, or aryl, $C(O)R_{20}$, $C(O)OR_{21}$ or $C(O)NR_{20}R_{22}$;~~

~~R_{23} = H, OR_{24}, alkyl, cycloalkyl, arylalkyl, aryl, $C(O)R_{25}$, $C(O)OR_{26}$ or $C(O)NR_{25}R_{27}$;~~

~~where R_{26} and R_{29} taken together can form a heterocyclic ring of 6 or 7 members;~~

~~or R_2 and R_4, R_2 and R_5, R_{10} and R_{11}, R_9 and R_{13}, R_{10} and R_{13}, R_9 and R_{14}, R_{11} and R_{14}, R_9 and R_{15}, R_{11} and R_{15}, R_{16} and R_{18}, R_{20} and R_{22}, R_{25} and R_{27}, R_{23} and R_{28}, R_{24} and R_{28}, R_{25} and R_{28}, R_{25} and R_{29}, R_{29} and R_{31} or R_{34} and R_{35} are optionally taken together to form a heterocyclic ring of 5 to 7 members;~~

E = O ~~or CH_2~~;

E_1 and E_2 independently are H or F; ~~or~~

~~E_1 and E_2, when taken together, form a carbon-carbon bond;~~

~~Y_1 = O or F, with the proviso that when Y_1 = F, then M_1 is absent; or~~

~~Y_1 represents a bond from the point of ring attachment to M_1;~~

~~Y_2 = O or F, with the proviso that when Y_2 = F, then M_2 is absent; or~~

~~Y_2 represents a bond from the point of ring attachment to M_2;~~

~~M_1 and M_2 are independently H, alkyl, cycloalkyl, arylalkyl, aryl, $C(O)M_3$, $C(O)OM_4$, or $C(O)NM_3M_5$;~~

~~M_3 = H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;~~

~~M_4 = alkyl, cycloalkyl, arylalkyl or aryl;~~

~~M_5 = H, alkyl, cycloalkyl, arylalkyl, or aryl; or~~

~~M_3 and M_5 taken together form a heterocyclic ring of 5 to 7 members;~~

~~when Y_1 = Y_2 = O, M_1 and M_2 optionally are bonds from the oxygen atoms of Y_1 and Y_2;~~

~~respectively, to a carbon atom of an acetal-, ketal- or orthoester group E_3;~~

~~wherein E_3 is $Q(A_1)(A_2)$;~~

~~wherein Q is a carbon atom;~~

~~A_1 = H, CF_3, alkyl, cycloalkyl, arylalkyl or aryl;~~

~~A_2 = H, OA_3, CF_3, alkyl, cycloalkyl, arylalkyl, aryl or heterocycle of 5 to 7 members;~~

~~A_3 = alkyl, cycloalkyl, arylalkyl or aryl; or~~

~~where A_1 and A_2, when taken together, form a carbocyclic ring of 5 or 6 members, with or without unsaturation, and with or without substitution; or~~

~~$M_1Q(A_1)(A_2)M_2$ is taken together to form a carbonyl bonded to Y_1 and Y_2, such that a cyclic carbonate is formed;~~

Y_1M_1 and Y_2M_2 are independently OH, F, or H;

Z = O, ~~NZ_3~~ NH, CH_2, CHF, CF_2, CCl_2, or CHCl;

Z_1 and Z_2 are independently O or S;

~~Z_3 = H, alkyl, cycloalkyl, arylalkyl, aryl or a heterocyclic ring of 5 to 7 members;~~

G_1 = O~~, S, CH_2 or $CH(OJ_1)$~~ or S;

G_2 = CH~~, $C(CH_2OJ_3)$, CCH_3, CCF_3, or $C(CO_2J_4)$~~;

G_3 = CH_2, CHF, CF_2, ~~$CH(OJ_5)$ or $CH(NJ_6J_7)$~~ CH(OH) or $CH(NHJ_7)$;

G_4 = CH_2, CHF, CF_2, ~~$CH(OJ_9)$, or $CH(NJ_{11}J_{13})$~~ CH(OH) or $CH(NHJ_{13})$;

G_5 = CH_2, CHF, CF_2, ~~$CH(OJ_{15})$, or $CH(NJ_{16}J_{17})$~~ CH(OH) or $CH(NHJ_{17})$;

G_6 = CH_2, ~~$CH(CH_3)$, $CH(CHF_2)$, $CH(CF_3)$, $CH(OJ_{19})$, $CH(CH_2OJ_{19})$,~~ $CH(CH_2OH)$;

~~$CH(CH_2(NJ_{21}J_{23}))$, or $CH(CO_2J_{22})$, with the provision that when G_1 = O or S, then G_6 does not equal CH(OH); and~~

the number of hydrogen atoms bonded to the G_1-G_6 ring atoms is limited to a maximum of 8; also with the provision that the number of nitrogen atoms bonded to the G_1-G_6 ring atoms in Formula I is limited to a maximum of 2;

~~J_1 = H, alkyl, cycloalkyl, arylalkyl, aryl, or $C(O)J_2$;~~

~~J_2, J_6, J_8, J_{10}, J_{11}, J_{14}, J_{16}, J_{18}, J_{20}, J_{22}, and J_{24} are independently H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;~~

~~J_3 = alkyl, cycloalkyl, arylalkyl, aryl or $C(O)J_2$;~~

~~J_4 = alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;~~

~~J_5 = H, alkyl, cycloalkyl, arylalkyl, aryl, or C(O)J_6;~~

J_7, J_{13}, and J_{17} ~~= H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J_8~~ are independently H, C(O)H, or C(O)alkyl;

~~J_9 = H, alkyl, cycloalkyl, arylalkyl, aryl, C(O)J_{10}, $CH(CH_3)(CO_2J_{11})$, or $CH(CH_3)(C(O)NJ_{11}J_{12})$;~~

~~J_{12} = H, alkyl, cycloalkyl, arylalkyl, aryl, heterocyclic ring of 5 to 7 members, an amino acid radical of 2 to 12 carbon atoms with or without hetero atoms, or a peptide radical comprising 2 to 10 amino acid units;~~

~~J_{13} = H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J_{14};~~

~~J_{15} = H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J_{16};~~

~~J_{17} = H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J_{18};~~

~~J_{19} = H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J_{20};~~

~~J_{21} = H, alkyl, cycloalkyl, arylalkyl, aryl, C(O)J_{22} or heterocyclic ring of 5 to 7 members;~~

~~J_{23} = H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J_{24}; or~~

~~J_6 and J_7, J_{11} and J_{12}, J_{11} and J_{13}, J_{16} and J_{17} or J_{21} and J_{23} are optionally taken together to form a heterocyclic ring of 5 to 7 members; or~~

~~where J_{22} and J_{24}, when taken together, form a heterocyclic ring of 5 to 7 members or a bicyclic imide comprising 4 to 12 carbons, with or without unsaturation and/or with or without substitution; or~~

~~when G_1 = $CH(OJ_1)$ and G_2 = $C(CH_2OJ_3)$, J_1 and J_3 optionally are bonds from the oxygen atoms of G_1 and G_2, respectively, to a carbon atom of an acetal , ketal- or orthoester group G_7; wherein G_7 = $Q_1(T_1)(T_2)$; or~~

~~when G_2 = $C(CH_2OJ_3)$ and G_3 = $CH(OJ_5)$, J_3 and J_5 optionally are bonds from the oxygen atoms of G_2 and G_3, respectively, to a carbon atom of an acetal , ketal- or orthoester group G_8; wherein G_8 = $Q_1(T_1)(T_2)$; or~~

~~when G_3 = $CH(OJ_5)$ and G_4 = $C(CHOJ_9)$, J_5 and J_9 optionally are bonds from the oxygen atoms of G_3 and G_4, respectively, to a carbon atom of an acetal , ketal- or orthoester group G_9; wherein G_9 = $Q_1(T_1)(T_2)$; or~~

~~when G_4 = $C(CHOJ_9)$ and G_5 = $CH(OJ_{15})$, J_9 and J_{15} optionally are bonds from the oxygen atoms of G_4 and G_5, respectively, to a carbon atom of an acetal , ketal- or orthoester group G_{10}; wherein G_{10} = $Q_1(T_1)(T_2)$; or~~